

Septic arthritis in malignancy

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Septic arthritis is an infection of a joint, which can be caused by bacteria, viruses, fungi, or parasites. The infection may happen in distant sites of the body, which then spread hematogenously, or it could also result from open wounds, surgery, or unsterile injections.¹ Septic arthritis is a serious condition that, if left undiagnosed and untreated, can cause joint destruction and an irreversible loss of joint function.^{2,3} Based on epidemiological data, the incidence of septic arthritis in general population is 2–10 cases in 100,000 people annually and is increased in those who have risk factors for septic arthritis, such as rheumatoid arthritis (RA) and joint prosthesis. In those with RA, the incidence of septic arthritis rises up to 30–70 cases in 100,000 people annually, and in those with prosthesis the figure is around 40–68 cases in 100,000 people annually.^{4,5} Septic arthritis can affect all age groups, but it is more prevalence in the elderly and in children under 5 years old, in which the prevalence is 8.4 and 5 cases, respectively, in 100,000 people annually.⁵ Septic arthritis is usually monoarticular, whereas polyarticular involvement occurs in only 10–15% of cases. The knee is involved in around 50% of cases.⁶

Septic arthritis is still a challenge for clinician since there has not been a significant decline in both morbidity and mortality in the last two decades.² Late recognition and therapy can cause permanent joint dysfunction and even death; thus, early diagnosis and prompt therapy is expected to decrease the morbidity and mortality rate in septic arthritis.⁶

In this case report we would like to present a case of a woman suffering from septic arthritis with an underlying immunocompromised condition of malignancy.

CASE REPORT

A 51-year-old woman was admitted to the Emergency Ward of Cipto Mangunkusumo General Hospital with a chief complaint of three-day history of tenderness on her left knee. The complaint had gradually worsened overtime and she also had difficulty in standing up and walking. The tenderness had acute onset, without any prior trauma, fever, or common cold. It was first felt when the patient was walking home from the hospital three days prior to admission, and initially she did not notice any changes on her left knee, but then after a while she noticed that her left knee had become swollen and felt warmer than the surrounding area. Up until this time, she was still able to stand up or walk,

although with minimal difficulty; however, in the day after the complaint worsened and the swelling of her knee became more apparent, the patient was no longer able to bend her knee without feeling excruciating pain. There was no prior history of morning stiffness in the affected knee.

She had been diagnosed for a nasopharyngeal carcinoma since 1 year prior to the admission, and at the time of admission she was undergoing her chemoradiation therapy. She had already had 4 cycles of chemotherapy and 17 sessions of radiation.

From the initial physical examination there was obtained data as follows: blood pressure of 110/80 mmHg, pulse rate of 88 beats/min, respiratory rate of 18 breaths/min, body temperature of 36.4°C; conjunctiva was rather pale; there were multiple lymph node enlargement on both sides of her neck with a diameter of 2 cm at most; her chest and abdominal physical examination were unremarkable. The examination of her extremities revealed a swollen left knee, which on palpation felt warmer than the surrounding area, with tenderness and pain in movement. The patient was also not able to bend the affected knee.

Early laboratory examination showed hemoglobin level of 10.3 g/dL, leukocyte count of $9.6 \times 10^3/\mu\text{L}$, serum urea of 28 mg/dL, serum creatinine of 1 mg/dL, serum uric acid of 4.7 mg/dL, aspartate aminotransferase (AST) of 21 U/L, alanine aminotransferase (ALT) of 18 U/L, and serum potassium of 3.0 mEq/L. A radiographic examination of her left knee showed signs of osteoarthritis (figure 1). Her chest radiograph was unremarkable.



Figure 1 Radiographic examination of the left knee (anteroposterior (left) and lateral view (right)), showing formation of osteophytes on lateral and medial intercondylar eminence and lateral condyle of tibia, lateral condyle of femur, and superior anterior, posterior, and inferior posterior aspect of patella.

From the data above, the initial problems established on the emergency ward were arthritis of left knee (which at first was suspected to be due to gout), nasopharyngeal carcinoma T4N3M0 (stage IVb) on chemoradiation, anemia due to chronic disease, and hypokalemia. Initial therapy given in the emergency ward were intravenous ringer lactate solution 500 mL/12 hours, intravenous methylprednisolone 8 mg b.i.d., colchicine 0.5 mg b.i.d., and potassium supplementation 1 tablet t.i.d. Sodium diclofenac was also added to her medication to alleviate the pain, which was initially given at 25 mg b.i.d. and later was increased to 50 mg b.i.d. At the time we planned to perform magnetic resonance imaging (MRI) and whole body bone scan to exclude the possibility of a metastatic process. We also decided to postpone the chemoradiation therapy considering the patient's condition.

A synovial fluid aspiration of the left knee was performed on the emergency ward and 1 mL of yellowish fluid was obtained. It was then sent for a synovial fluid analysis, but unfortunately there was not enough sample for the analysis. The patient was then admitted to the inpatient ward.

On the third day after admission, MRI of her left knee joint was performed, showing arthrosis, synovitis, and degeneration of medial meniscus of the left knee joint (figure 2).

On the fourth day after admission, an arthrocentesis on the left knee joint was performed, which resulted in 10 mL of thick yellowish synovial fluid. The sample was subsequently sent to the laboratory for a culture and cytology examination, and it was then reassessed that the arthritis on her left knee joint was due to septic arthritis. The intravenous methylprednisolone and colchicine were stopped, and the patient was started with antibiotic therapy with levofloxacin 500 mg q.d. and ceftazidime 1 g t.i.d. An arthroscopic debridement of her left knee joint was also planned, but it was subsequently postponed due to financial problem. It was then decided that this procedure would be performed if the patient could get a free arthroscopy equipment from the Department of Orthopedics.

On the fifth day after admission, tramadol infusion in 500 mL normal saline b.i.d. was added to her medication because

sodium diclofenac alone was not able to suppress her pain. Arthrocentesis was performed again on her left knee, which at this time resulted in 2 mL of yellowish synovial fluid that was sent for culture and cytology examination.

On the eighth day after admission, whole body bone scan was performed, showing no signs of metastasis to the bone.

On the ninth day, the cytology report showed only macrophage and leukocytes without any sign of malignant tumor cell. The culture showed that the bacterium infecting her knee joint was *Streptococcus anhemolyticus*, which was sensitive to amoxicillin/clavulanate, levofloxacin, and ceftazidime. The patient then received intravenous levofloxacin and ceftazidime for 14 days, followed with oral amoxicillin/clavulanate.

In the following days, the pain and tenderness of her left knee began to alleviate, accompanied by improvement of her range of motion; nevertheless, the patient was told not to use her left limb in weight-bearing activities.

On the sixteenth day after admission, an arthrocentesis procedure was reperformed, but this time it resulted in a dry tap. The plan to do an arthroscopy on her left knee was still unable to be carried out due to financial and scheduling problem, but it was decided that she could be discharged after completing her 14-day regimen of intravenous antibiotic therapy considering the improvement of her condition. Chemotherapy for the nasopharyngeal carcinoma could then recommence.

On the twenty second day after admission, the patient was discharged and her antibiotic therapy was continued with oral amoxicillin/clavulanate 650 mg t.i.d.

DISCUSSION

The symptom of joint pain is associated with a wide variety of disorder. Pain due to a problem within the joint needs to be distinguished from pain from nearby soft tissues or juxta-articular bone. If joint motion is preserved but tenderness can be elicited by palpation over one of the regional bursae, tendons, or ligaments, it is unlikely that the joint pain is due to arthritis. Arthritis is likely when the pain is aggravated by



Figure 2 Magnetic resonance imaging of the left knee, showing degeneration of medial meniscus (A), accumulation of synovial fluid (B), and formation of osteophytes on medial epicondyle of femur, medial and lateral epicondyle of tibia, and intercondylar eminence (C).

movement, associated with loss of motion, and accompanied by swelling and/or erythema.⁷

The initial diagnostic evaluation of the patient with monoarticular arthritis should focus upon the possibility of an infectious etiology. Infection is a relatively common cause of acute pain and swelling in a single joint that can result in cartilage destruction within a few days if unrecognized; thus, while the history and physical examination provide important clinical clues, a definitive diagnosis often requires early performance of arthrocentesis and synovial fluid analysis.^{1,8} The algorithm for the therapeutic approach to a suspected bacterial arthritis is shown in figure 3.

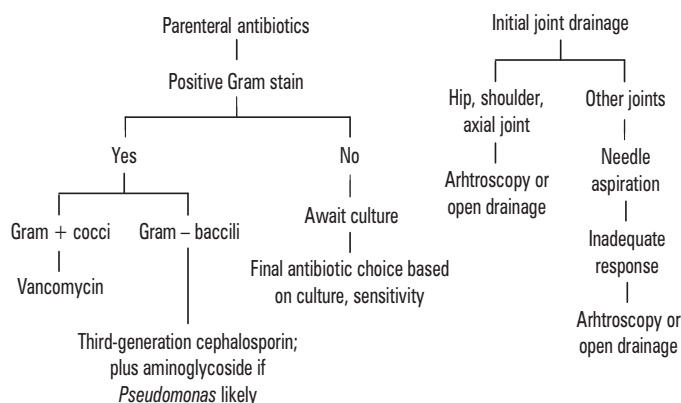


Figure 3 Algorithm for antibiotics selection and joint drainage in bacterial arthritis.⁶

In this case report, the patient had tenderness on a single joint, which is the knee joint; the pain was aggravated by movement, associated with loss of motion, and accompanied by swelling and/or erythema. The planned initial diagnostic modalities in the inpatient ward were MRI and bone scan due to suspicion of a metastatic process in her left knee. Besides, arthrocentesis procedure was also carried out with culture and cytology examination of the obtained synovial fluid. Subsequently, the result was septic arthritis with *Streptococcus anhemolyticus* as the identified pathogen.

Bacterial arthritis can result from a bite or other trauma, from direct inoculation of bacteria during joint surgery, or rarely, when infection of bone adjacent to the joint extends through the cortex into the joint space. However, in most cases, bacterial arthritis arises from hematogenous spread to the joint. Patients with hematogenously-induced bacterial arthritis may present with joint abnormalities in the absence of signs of sepsis or bacteremia. These patients presumably acquired their infection from a transient or self-limiting bacteremia.⁹

Predisposing factors for septic arthritis in adults were identified in a 2007 systematic review that included a total of 6,242 patients with acutely painful joints; 653 (10 percent) had septic arthritis and the predisposing factors and associated value as predictors (reflected by the estimated positive likelihood ratios) are summarized as follows: age greater than 80 years, diabetes mellitus, RA, prosthetic joint, recent joint surgery, skin infection and cutaneous ulcers, intravenous drug abuse and alcoholism, and previous intra-articular corticosteroid injection.^{6,12}

Patients with bacterial arthritis present acutely with a single swollen and painful joint (i.e., monoarticular arthritis). The knee is involved in more than 50 percent of cases but wrists, ankles, and hips are also commonly infected.¹⁰

Joint pain, swelling, warmth, and restricted movement are self-reported by a majority of patients. These symptoms were noted at presentation in 85 and 78 percent, respectively, of patients with septic arthritis. A majority of patients with bacterial arthritis are febrile, although chills and spiking fevers are unusual.¹¹

The most important laboratory test in the evaluation of monoarticular joint pain is synovial fluid analysis. Arthrocentesis should be attempted in all patients who have an effusion or signs suggesting inflammation within the joint.⁸

Virtually, any microbial pathogen is capable of causing bacterial arthritis. However, organisms such as *Staphylococcus aureus* and *Streptococci* have a higher propensity to cause joint infections than Gram-negative bacilli, which typically only produce these infections after trauma or in patients with severe underlying immunosuppression.⁹

MRI could be used as an early diagnostic tool, which could show an image of swollen and compression of the joint soft tissue.¹²

Treatment of acute bacterial arthritis requires appropriate antimicrobials and adequate joint drainage (figure 3).⁹

No randomized controlled studies have evaluated antibiotic regimens for bacterial arthritis. The initial choice of antimicrobial regimens is based on the coverage of the most likely organisms to cause infection. There have been no controlled trials examining the duration of antimicrobial therapy in bacterial arthritis. Treatment recommendations are based on clinical case series and cannot be generalized for all patients. Usually parenteral antibiotics are given for at least 14 days followed by oral therapy (if possible) for an additional 14 days.⁹

If the synovial fluid is purulent and/or bacteria is found on Gram's staining, prompt wide spectrum antibiotic therapy should be given. Based on the most prevalent bacterium that causes septic arthritis, which is *S. aureus*, the first choice of antibiotics are intravenous penicillin G, cloxacillin, clindamycin, or netilmicin. A de-escalation therapy must be commenced after the result from synovial fluid culture is obtained.¹²

No randomized controlled studies have evaluated joint drainage procedures in adults for bacterial arthritis; thus, recommendations are based on small retrospective studies and are dependent on the joint affected and the time from onset of infection until evaluation. Although no studies have compared drainage with no-drainage procedure, we recommend joint drainage in all patients with septic arthritis as this condition represents a closed abscess collection. The three procedures used are needle aspiration (single or multiple), arthroscopic drainage, or arthrotomy (open surgical drainage).⁹

Most peripheral joints can be drained with closed needle aspiration, although daily aspiration may be necessary.¹² If adequate drainage cannot be obtained by needle aspiration, either arthroscopy or open drainage is necessary. For knee, shoulder, and wrist infections, arthroscopy is often preferred

because of easier irrigation and better visualization of the joint.¹³

CONCLUSION

Septic arthritis due to bacterial pathogens is the most potentially dangerous and destructive form of acute arthritis; thus, early diagnosis and prompt therapy is very crucial in reducing morbidity and mortality due to septic arthritis. Patient presenting with acute pain, which aggravated by movement, associated with loss of motion, and accompanied by swelling and/or erythema mostly on a single joint should be suspected

for septic arthritis. Synovial fluid analysis is an important diagnostic procedure. Prompt therapy with broad spectrum antibiotic is a must when a purulent synovial fluid is obtained from arthrocentesis. The prognosis of bacterial arthritis has not improved significantly in the past few decades, despite better antibiotics and drainage. It is extremely difficult to predict the functional outcome of individual patients during and at the conclusion of treatment. The outcome is directly related to host factors, such as prior joint damage, the virulence of the infecting organism, and the speed with which adequate treatment is begun.

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